Renpenning syndrome

Renpenning syndrome is a disorder that almost exclusively affects males, causing developmental delay, moderate to severe intellectual disability, and distinctive physical features. Individuals with Renpenning syndrome typically have short stature and a small head size (microcephaly). Facial features characteristic of this disorder include a long, narrow face; outside corners of the eyes that point upward (upslanting palpebral fissures); a long, bulbous nose with a low-hanging separation between the nostrils (overhanging columella); a shortened space between the nose and mouth (philtrum); and cup-shaped ears. Males with Renpenning syndrome generally have small testes. Seizures and wasting away (atrophy) of muscles used for movement (skeletal muscles) may also occur in this disorder.

About 20 percent of individuals with Renpenning syndrome also have other features, which may include a gap or split in structures that make up the eye (coloboma), an opening in the roof of the mouth (cleft palate), heart abnormalities, or malformations of the anus.

Certain combinations of the features that often occur in Renpenning syndrome are sometimes called by other names, such as Golabi-Ito-Hall syndrome or Sutherland-Haan syndrome. However, all these syndromes, which have the same genetic cause, are now generally grouped under the term Renpenning syndrome.

Frequency

Renpenning syndrome is a rare disorder; its prevalence is unknown. More than 60 affected individuals in at least 15 families have been identified.

Genetic Changes

Renpenning syndrome is caused by mutations in the *PQBP1* gene. This gene provides instructions for making a protein called polyglutamine-binding protein 1. This protein attaches (binds) to stretches of multiple copies of a protein building block (amino acid) called glutamine in certain other proteins.

While the specific function of polyglutamine-binding protein 1 is not well understood, it is believed to play a role in processing and transporting RNA, a chemical cousin of DNA that serves as the genetic blueprint for the production of proteins.

In nerve cells (neurons) such as those in the brain, polyglutamine-binding protein 1 is found in structures called RNA granules. These granules allow the transport and storage of RNA within the cell. The RNA is held within the granules until the genetic information it carries is translated to produce proteins or until cellular signals

or environmental factors trigger the RNA to be degraded. Through these mechanisms, polyglutamine-binding protein 1 is thought to help control the way genetic information is used (gene expression) in neurons. This control is important for normal brain development.

Most of the mutations in the *PQBP1* gene that cause Renpenning syndrome result in an abnormally short polyglutamine-binding protein 1. The function of a shortened or otherwise abnormal protein is likely impaired and interferes with normal gene expression in neurons, resulting in abnormal development of the brain and the signs and symptoms of Renpenning syndrome.

Inheritance Pattern

This condition is inherited in an X-linked recessive pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation typically has to occur in both copies of the gene to cause the disorder. Because it is unlikely that females will have two altered copies of this gene, males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

Other Names for This Condition

- Golabi-Ito-Hall syndrome
- Hamel cerebropalatocardiac syndrome
- Porteous syndrome
- Sutherland-Haan syndrome
- X-linked intellectual deficit due to PQBP1 mutations
- X-linked intellectual deficit, Renpenning type

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Renpenning syndrome 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796135/

Other Diagnosis and Management Resources

- Greenwood Genetics Center: X-Linked Intellectual Disability
  http://www.ggc.org/diagnostic/tests-costs/test-finder/test-finder.html?id=242
- Kennedy Krieger Institute: Center for Genetic Disorders of Cognition and Behavior
  http://gcbcenter.kennedykrieger.org/xmr.jsp

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html

Genetic and Rare Diseases Information Center

- Renpenning syndrome 1
  https://rarediseases.info.nih.gov/diseases/9509/renpenning-syndrome-1

Educational Resources

- Centers for Disease Control: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Disease InfoSearch: Renpenning syndrome 1
  http://www.diseaseinfosearch.org/Renpenning+syndrome+1/6224
- MalaCards: renpenning syndrome
  http://www.malacards.org/card/renpenning_syndrome
- Orphanet: Renpenning syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=3242

Patient Support and Advocacy Resources

- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/devdelay.html

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Renpenning+syndrome%22+OR+%22Mental+Retardation%2C+X-Linked%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28renpenning+syndrome%5BTIAB%5D%29+OR+%28rens1%5BTIAB%5D%29+OR+%28sutherland-haan+syndrome%5BTIAB%5D%29+OR+%28golabi-ito-hall+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

OMIM

- RENPENNING SYNDROME 1
  http://omim.org/entry/309500

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